Looking for new xanthine oxidase inhibitors: 3-Phenylcoumarins versus 2-phenylbenzofurans

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Overproduction of uric acid in the body leads to hyperuricemia, which is also closely related to gout. Uric acid production can be lowered by xanthine oxidase (XO) inhibitors. Inhibition of XO has also been proposed as a mechanism for improving cardiovascular health. Therefore, the search for new efficient XO inhibitors is an interesting topic in drug discovery. 3-Phenylcoumarins and 2-phenylbenzofurans are privileged scaffolds in medicinal chemistry. Their structural similarity makes them interesting molecules for a comparative study. Methoxy and nitro substituents were introduced in both scaffolds. The current study gives some insights into the synthesis and biological activity of these molecules against this important target. For the best compound of the series, the 3-(4-methoxyphenyl)-6-nitrocoumarin (4), the IC50 value, type of inhibition, cytotoxicity on B16F10 cells and ADME theoretical properties, were determined. Docking studies were also performed in order to better understand the interactions of this molecule with the XO binding pocket. This work is a preliminary screening for further design and synthesis of new non-purinergic derivatives as potential compounds involved in the inflammatory suppression, specially related to gout.

2-Phenylbenzofurans

3-Phenylcoumarins

Xanthine oxidase inhibitors

2 hydroxybenzylalcohol derivative

2 hydroxybenzyltriphenylphosphonium bromide

2 phenylbenzofuran

2 phenylbenzofuran derivative

3 arylcoumarin derivative

3 phenylcoumarin derivative

allopurinol

benzofuran derivative

coumarin derivative

febuxostat

unclassified drug

xanthine oxidase

xanthine oxidase inhibitor

animal cell

Article

chromatography

concentration (parameter)

controlled study

cytotoxicity

drug receptor binding

enzyme inhibition

evaporation

IC50

molecular docking

mouse

nonhuman

particle size

physical chemistry

thin layer chromatography